

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference FOR FURTHER see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.				
PU4758WO ACTION				
International application No.				
PCT/US 03/22717	/US 03/22717 21/07/2003 23/07/2002			
Applicant				
SMITHKLINE BEECHAM CORPORA	ATION			
This International Search Report has bee according to Article 18. A copy is being tra	n prepared by this International Searching Aut ansmitted to the International Bureau.	hority and is transmitted to the applicant		
This International Search Report consists	of a total of 8 sheets.			
	a copy of each prior art document cited in this	report.		
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Basis of the report	international search was carried out on the ba	sis of the international application in the		
a. With regard to the language, the language in which it was filed, un	less otherwise indicated under this item.	sis of the international application in the		
the international search v Authority (Rule 23.1(b)).	vas carried out on the basis of a translation of	the international application furnished to this		
b. With regard to any nucleotide as	nd/or amino acid sequence disclosed in the i	nternational application, the international search		
was carried out on the basis of th	ne sequence listing: onal application in written form.			
	ernational application in computer readable for	m.		
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furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readble form.				
the statement that the su	the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the			
	international application as filed has been furnished. the statement that the information recorded in computer readable form is identical to the written sequence listing has been			
furnished	official of recorded in computer readable form	3		
2. X Certain claims were for	und unsearchable (See Box I).			
3. Unity of invention is lacking (see Box II).				
4. With regard to the title,				
	submitted by the applicant.			
the text is approved as submitted by the applicant. the text has been established by this Authority to read as follows:				
5. With regard to the abstract,				
His to the an establish	submitted by the applicant. lished, according to Rule 38 2(b), by this Autho	ority as it appears in Box III. The applicant may,		
x the text has been estable within one month from the	he date of mailing of this international search re	eport, submit comments to this Authority.		
6. The figure of the drawings to be pu	blished with the abstract is Figure No.			
as suggested by the ap	plicant.	None of the figures.		
because the applicant for	ailed to suggest a figure.			
because this figure better characterizes the invention.				



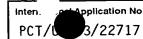
Internal application No.

PCT/US 03/22717

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present invention relates to inhibitors of the kinases GSK3 or more particularly to pyrazolopyrimidine compounds useful as kinase	TIE2, and inhibitors.

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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/519 A61P3/06 A61P9/12 A61P5/48 A61P9/10 A61P37/04 A61P35/00 A61P25/28 A61P17/14 A61P15/08 A61P43/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\label{lem:minimum} \begin{array}{ll} \text{Minimum documentation searched (classification system followed by classification symbols)} \\ \text{IPC 7} & \text{A61K} \end{array}$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

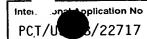
EPO-Internal, CHEM ABS Data, WPI Data

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00 38675 A (HOLDER JULIE CAROLINE; SMITH DAVID GLYNN (GB); COGHLAN MATTHEW PAU) 6 July 2000 (2000-07-06) cited in the application abstract page 1, paragraph 1 - paragraph 4 page 2, paragraph 3 page 5, paragraph 4 page 11, paragraph 3 -page 13, paragraph 2	1-20
Α	US 5 593 997 A (DOW ROBERT L ET AL) 14 January 1997 (1997-01-14) abstract column 1, paragraph 1 column 2, line 18 -column 4, line 25 column 11, paragraph 5 -column 12, paragraph 5 claims 1-16	1-20

Further documents are listed in the continuation of box C.	χ Patent family members are listed in annex.
Special categories of cited documents: A' document defining the general state of the art which is not considered to be of particular relevance E' earlier document but published on or after the international filing date 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) 'O' document referring to an oral disclosure, use, exhibition or other means 'P' document published prior to the international filing date but later than the priority date claimed	 *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. *8* document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
17 December 2003	30/12/2003
Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Langer, O

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		PC,T/U	5/22717
.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT		
ategory °	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.
A	WO 01 19829 A (BASF AG; HIRST GAVIN C (US); RAFFERTY PAUL (US); RITTER KURT (US);) 22 March 2001 (2001-03-22) abstract page 7, paragraph 3 -page 8, paragraph 3 page 14 -page 18		1-20
	WO 98 14449 A (CIBA GEIGY AG ;TRAXLER PETER (CH); BOLD GUIDO (CH); FREI JOERG (CH) 9 April 1998 (1998-04-09) abstract page 1, paragraph 1 page 5, paragraph 4 -page 6, paragraph 2		1-20
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

- a) Dependent claims 16-18 have been drafted as method claims but refer to use claim 14. They have been assumed to read "The use of claim 14 (...)", cf. page 8, lines 25-30.
- b) The expression "serine/threosine kinase" in claims 8 and 15 has been searched as reading "serine/threonine kinase", cf. page 3, line 18 of the description.
- c) The expression "piperadinyl" in claim 4 has been searched as reading "piperidinyl", cf. page 7, line 31 of the description.
- d) The expressions "disease or condition characterized by misregulation of a protein kinase" in claims 1, 14 and dependent claims and the further specifications of the kinase being "a serine/threosine kinase" (claims 8 and 15), "GSK3" (claims 9 and 16), "a tyrosine kinase" (claims 10 and 17), and "TIE2" (claims 11 and 18) lack clarity within the meaning of Article 6 PCT because it is unclear which specific pathological conditions (diseases) and indications do fall within this mechanistic definition and which do not.
- e) The expression "pharmaceutically acceptable derivatives" in present claims 1, 14 and dependent claims relates to compounds defined by reference to a desirable characteristic or property, namely their capability to provide "upon administration to a mammal '...! (directly or indirectly) a compound of the present invention or an active metabolite thereof" (page 11, line 30 to page 12, line 2).

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

f) Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use of compounds according to formula (I) in the treatment of a pathological condition (disease) selected from the group consisting of type 2 diabetes, hyperlipidemia, obesity, CNS disorders, neurotraumatic injuries, baldness or hair loss, atherosclerotic cardiovascular disease, hypertension, polycystic ovary syndrome, ischemia, immunodeficiency and cancer or to provide immune potentiation.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.





Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	rnational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. χ	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Although claims 1-13 and 20 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. X	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
	see FURTHER INFORMATION sheet PCT/ISA/210
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remai	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

INTERN ONAL SEARCH REPORT

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n on patent family members

PCT/U. 3/22717

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 0038675	А	06-07-2000	AU EP WO	1877700 A 1140070 A1 0038675 A1	31-07-2000 10-10-2001 06-07-2000
US 5593997	Α	14-01-1997	NONE		
WO 0119829	Α	22-03-2001	AT AU BG BR CA CN CZ DE EP JP NO SK TR WO US US	247657 T 7495000 A 106586 A 0014073 A 2385747 A1 1390220 T 20020936 A3 60004685 D1 1212327 A2 2003509428 T 20021328 A 3812002 A3 200201505 T2 0119829 A2 6660744 B1 2002156081 A1	15-09-2003 17-04-2001 31-01-2003 16-07-2002 22-03-2001 08-01-2003 16-10-2002 25-09-2003 12-06-2002 11-03-2003 21-05-2002 11-09-2003 21-01-2003 22-03-2001 09-12-2003 24-10-2002
 WO 9814449	Α	09-04-1998	AU AU WO WO ID ZA	4706997 A 4779897 A 9814449 A1 9814451 A1 18494 A 9708801 A	24-04-1998 24-04-1998 09-04-1998 09-04-1998 16-04-1998 02-04-1998